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FULL ESTIMATED COST	0.21	0.21

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FILE 'USPATFULL' ENTERED AT 15:12:55 ON 21 JUL 2003
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=> c-peptide(5A)insulin
L1 1962 FILE CAPLUS
L2 3142 FILE BIOSIS
L3 2915 FILE MEDLINE
L4 2922 FILE EMBASE
L5 266 FILE USPATFULL

TOTAL FOR ALL FILES
L6 11207 C-PEPTIDE(5A) INSULIN

=> antibody same l6 same sheep
MISSING OPERATOR SAME L6
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> antibody(P)l6
L7 125 FILE CAPLUS
L8 230 FILE BIOSIS
L9 228 FILE MEDLINE
L10 269 FILE EMBASE
L11 47 FILE USPATFULL

TOTAL FOR ALL FILES
L12 899 ANTIBODY(P) L6

=> sheep(P)l12
L13 1 FILE CAPLUS
L14 0 FILE BIOSIS
L15 0 FILE MEDLINE
L16 0 FILE EMBASE
L17 0 FILE USPATFULL

TOTAL FOR ALL FILES
L18 1 SHEEP(P) L12

=> d l18 ibib abs total

L18 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:320215 CAPLUS
DOCUMENT NUMBER: 134:339540
TITLE: A new immunologic assay to determine C-peptide containing impurities in samples of human insulin and derivatives thereof
INVENTOR(S): Gerl, Martin; Steinert, Cornelia
PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001031336	A2	20010503	WO 2000-EP10482	20001025
WO 2001031336	A3	20011108		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1228374	A2	20020807	EP 2000-974449	20001025
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003513243	T2	20030408	JP 2001-533423	20001025

PRIORITY APPLN. INFO.: DE 1999-19951684 A 19991027
WO 2000-EP10482 W 20001025

AB The invention relates to a process for detecting or detg. a C-peptide-contg. impurity in a sample of recombinantly produced human insulin or a deriv. thereof, by a non-radioactive assay, comprising the steps: (a) prepg. a sample of recombinantly produced human insulin or a deriv. thereof; (b) mixing the samples with diln. buffer; (c) adding a tracer to mixt. (b); (d) adding antibody specific for the C-peptide impurity to mixt. (c); (e) adding "C-peptide second antibody bead" having at least one label to mixt. (d); and (f) detecting or detg. the presence of the C-peptide-contg. impurity.

=> l12(P)preproinsulin
L19 0 FILE CAPLUS
L20 1 FILE BIOSIS
L21 1 FILE MEDLINE
L22 1 FILE EMBASE
L23 1 FILE USPATFULL

TOTAL FOR ALL FILES
L24 4 L12(P) PREPROINSULIN

=> dup rem
ENTER L# LIST OR (END):l24
PROCESSING COMPLETED FOR L24
L25 3 DUP REM L24 (1 DUPLICATE REMOVED)

=> l25 same both
MISSING OPERATOR L25 SAME
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

```
=> l25(P)both
L26           0 S L25
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L26(P)BOTH'
L27           0 FILE CAPLUS
L28           1 S L25
L29           1 FILE BIOSIS
L30           0 S L25
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L30(P)BOTH'
L31           0 FILE MEDLINE
L32           1 S L25
L33           0 FILE EMBASE
L34           1 S L25
L35           0 FILE USPATFULL

TOTAL FOR ALL FILES
L36           1 L25(P) BOTH

=> l25(P)recognize(P)preproinsulin
L37           0 S L25
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L37(P)RECOGNIZE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'RECOGNIZE(P)PREPROINSU'
L38           0 FILE CAPLUS
L39           1 S L25
L40           0 FILE BIOSIS
L41           0 S L25
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L41(P)RECOGNIZE'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'RECOGNIZE(P)PREPROINSU'
L42           0 FILE MEDLINE
L43           1 S L25
L44           0 FILE EMBASE
L45           1 S L25
L46           0 FILE USPATFULL

TOTAL FOR ALL FILES
L47           0 L25(P) RECOGNIZE(P) PREPROINSULIN

=> d l25 ibib abs total

L25  ANSWER 1 OF 3  USPATFULL on STN
ACCESSION NUMBER:        89:65035  USPATFULL
TITLE:                   Method of detecting antibodies
INVENTOR(S):             Soeldner, J. Stuart, Newton, MA, United States
PATENT ASSIGNEE(S):      Joslin Diabetes Center, Inc., Boston, MA, United States
                         (U.S. corporation)

                            NUMBER        KIND    DATE
                         --------------- ------ --------
PATENT INFORMATION:      US 4855242              19890808
APPLICATION INFO.:       US 1987-680             19870106  (7)
RELATED APPLN. INFO.:    Continuation-in-part of Ser. No. US 1986-851482, filed
                         on 14 Apr 1986, now abandoned
DOCUMENT TYPE:           Utility
FILE SEGMENT:            Granted
PRIMARY EXAMINER:        Warden, Robert J.
ASSISTANT EXAMINER:      Benson, Robert
NUMBER OF CLAIMS:        29
EXEMPLARY CLAIM:         1
```

NUMBER OF DRAWINGS: 2 Drawing Figure(s); 2 Drawing Page(s)
LINE COUNT: 545
AB A method for determining the quantity of an antibody in a sample, the method having the steps of: (1) providing a labelled antigen to the antibody; (2) contacting the labelled antigen with the sample in solution to form a labelled antigen-antibody complex; (3) providing an agent for precipitating the complex; (4) mixing the solution containing the labelled antigen-antibody complex with the precipitating agent to produce a precipitate and a supernatant; the supernatant containing labelled antigen and the precipitate containing the labelled antigen-antibody complex and uncomplexed labelled antigen; and (5) measuring the quantity of label in the precipitate or the supernatant in a manner substantially independent of the amount of uncomplexed labelled antigen in the precipitate.

L25 ANSWER 2 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
ACCESSION NUMBER: 1989:290457 BIOSIS
DOCUMENT NUMBER: BA88:15801
TITLE: PANCREATIC HORMONES ARE EXPRESSED ON THE SURFACES OF HUMAN AND RAT ISLET CELLS THROUGH EXOCYTOTIC SITES.
AUTHOR(S): LARSSON L-I; NIELSEN J H; HUTTON J C; MADSEN O D
CORPORATE SOURCE: DEP. MOL. CELL BIOL., STATE SERUM INST., BUILD. 81, AMAGER BLVD. 80, DK-2300 COPENHAGEN S, DEN.
SOURCE: EUR J CELL BIOL, (1989) 48 (1), 45-51.
CODEN: EJCBDN. ISSN: 0171-9335.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Human and rat insulin cells show insulin immunoreactivity, and glucagon cells show glucagon immunoreactivity on their membrane surfaces, respectively. The reaction occurs in the form of small dots on the islet cell surface and colocalizes with the chromogranin family of secretory granule markers. Electron microscopy reveals the labeling to occur at sites of exocytotic granule release, involving the surfaces of extruded granule cores. The surfaces of islet cells were labeled both by polyclonal and monoclonal **antibodies**, excluding that receptor-interacting, anti-idiotypic hormone **antibodies** were responsible for the staining. Human insulin cells were surface-labeled by monoclonal **antibodies** recognizing the mature secretory products, **insulin** and **C-peptide** but not with monoclonal **antibodies** specific for proinsulin. Thus, routing of unprocessed **preproinsulin** to the cell surface may not account for these results. It is concluded that the staining reflects interactions between the appropriate **antibodies** and exocytotic sites of hormone release.

L25 ANSWER 3 OF 3 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 86257013 EMBASE
DOCUMENT NUMBER: 1986257013
TITLE: C-peptide: An index of insulin secretion.
AUTHOR: Faber O.K.; Binder C.
CORPORATE SOURCE: Medical Department, Horsholm Hospital, Copenhagen, Denmark
SOURCE: Diabetes/Metabolism Reviews, (1986) 2/3-4 (331-345).
CODEN: DMREEG
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 006 Internal Medicine
029 Clinical Biochemistry
003 Endocrinology
LANGUAGE: English
AB The clinical course of insulin-dependent diabetes mellitus (IDDM) indicates a progressive, rapid, and profound loss of beta cell function in most cases. However, partial and even complete clinical remissions

demonstrate the regenerative capacity of beta cell function in some patients. Delineation of the insulin biosynthetic pathway from **preproinsulin** to proinsulin to **insulin/C-peptide** has provided the investigator with the means for following the natural history of IDDM. Since **insulin** and **C-peptide** are secreted in equimolar amounts by the beta cells, measurement of circulating C-peptide levels has provided an innovative way of evaluating beta cell function during insulin treatment of IDDM patients. Until the development of C-peptide assays, the evaluation of beta cell function has been hampered by the inability of insulin assays to discriminate between endogenous and exogenous insulin, as well as by the formation of insulin **antibodies** that interfere with the measurement of plasma insulin concentration by standard radioimmunoassay procedures. In this review we will discuss methodologic aspects of the C-peptide assay, together with the insight into the natural history of beta cell function in IDDM patients, that have been obtained using this assay.